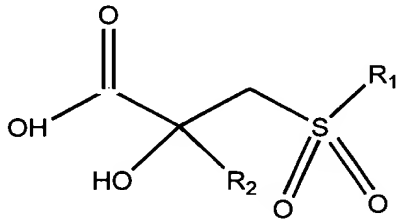
REMARKS

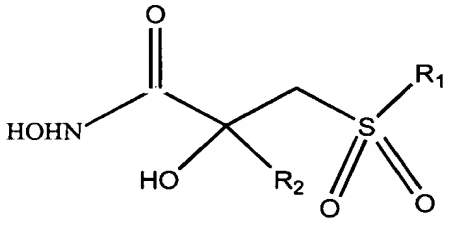
Responsive to the Official Action mailed October 2, 2003, the Examiner's comments have been studied. Claims 4, 20-25 and 31-36 are currently pending. In view of the following remarks, the application is submitted as being in condition for allowance.

Claims 4, 20-25 and 31-36 are active. Claim 4 was previously amended. Claims 4, 20-25 and 31-36 are finally rejected under 35 U.S.C. § 103(a) as obvious over the "deprotection" product found in scheme 1, page 95 of Freskos et al. (WO 98/39326).

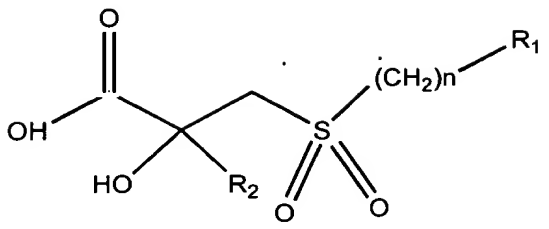
The Examiner states that Freskos et al. (WO 98/39326) teaches a generic group of compounds which embraces compounds here claimed and for this proposition cites scheme 1, page 95 of the reference, presumable for its disclosure of the "deprotection" product of



Presumably, the R_1 and R_2 of such "deprotection" product is the same R_1 and R_2 as the Freskos reference teaches for its claimed compounds of the formula



The Examiner states that one of skill in the art would have been motivated to modify this "deprotection" compound by inserting an alkylene group (-$(CH_2)_n$- ; n = 1, 2,3, etc) between the sulfur atom and the R_1 group of this "deprotection" compound because varying the size of a linking carbon chain is *per se* obvious. According to the Examiner's argument Freskos makes the following compound obvious:



However, to insert an alkylene group between the sulfur atom and the R_1 group of this Freskos compound would be directly against the teaching of the Freskos reference. Freskos at page 8, line 20 – page 9, line 19 and page 12, line 15 – page 16, line 15 states that :

> R_1 is a substituent that contains a 5- or 6-membered cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical **bonded directly to the depicted SO_2 -group** and having a length greater than about that of a fully extended hexyl group and less than about that of a fully extended eicosyl group. In addition, R_1 defines a three-dimensional volume, when **rotated about an axis drawn through the SO_2 -bonded 1-position and the 4-position of a 6-membered ring radical or drawn through the SO_2 -bonded 1-position and the center of 3,4-bond of a 5-membered ring radical**, whose widest dimension in a direction transverse to the axis of rotation is about that of one furanyl ring to about that of two phenyl rings.
>
> R_1 preferably contains a single aromatic or heteroaromatic ring that is itself substituted with another substituent, R_3. R_1 most preferably contains a phenyl ring, Ph, that is itself has a substituent, R_3, at the 4-position. R_3 is preferably a phenyl, a phenoxy, a phenylazo, a thiophenoxy, an anilino, a benzamido, a nicotinamido, an isonicotinamido, a picolinamido or an ureidophenyl group that can itself be substituted at the meta- or para-position or both by a single atom or a substituent containing a longest chain of up to eight atoms, excluding hydrogen. [Emphasis Added].

Further Freskos makes clear at page 16, lines 14-17 that the R_1 group is :

> **An SO_2 -linked cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical** is a 5- or 6-membered single-ring that is itself substituted with one other substituent, R_3. The **SO_2 -linked single-ringed cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical** is R_3 -substituted at its own 4-position when a 6-membered ring and at its own 3-position when a 5-membered ring. [Emphasis Added].

Were Freskos permissive of an alkylene link between the sulfur atom and the R_1 group of this "deprotection" compound, then there may be some viability to the Examiner's argument that varying the size of a linking carbon chain is *per se* obvious. However, Freskos is expressly not permissive of an alkylene link between the sulfur atom and the R_1 group of this "deprotection" compound. Freskos expressly requires the 5- or 6-membered

cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical (R_1) to be bonded directly to the depicted SO_2 –group. The Examiner's reconstruction and redesign of the Freskos compound to include an alkylene link between the sulfur atom and the R_1 group, which is contrary to the express teaching of Freskos, is improper. *In re Ratti*, 123 USPQ 349, 352 (CCPA 1959); *In re Schulpen*, 157 USPQ 52, 55 (CCPA 1968). The mere fact that the Freskos could be modified by inserting an alkylene group between the sulfur atom and the R_1 group of this "deprotection" compound would not have made the modification obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, Freskos itself diverges from and teaches away from an alkylene link between the sulfur atom and the R_1 group, hence it is error for the Examiner to argue that such alkylene link between the sulfur atom and the R_1 group is obvious in the Freskos compound. *In re Fine*, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988); and *In re Fritch*, 23 USPQ2d 1780, 1783 fn 12 (Fed. Cir. 1992).

To establish a prima facie case of obviousness, the Examiner must show "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fine*, 5 USPQ2d at 1598. There is no suggestion to combine, however, if a reference teaches away from its combination with another source. *In re Fine*, 5 USPQ2d at 1599. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant . . . [or] if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). If when combined, the references "would produce a seemingly inoperative device," then they teach away from their combination. *In re Sponnoble*, 160 USPQ 237, 244 (CCPA 1969); see also *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984) (finding no suggestion to modify a prior art device where the modification would render the device inoperable for its intended purpose).

In first stating the basis for rejection under 35 USC § 103, the Examiner stated that the R_1 group of the deprotection product of Freskos "is cycloalkyl, heterocycle, aryl, etc." whereas the R_2 group "is hydrocarbyl, (N-morpholino)methyl, (N-pyrrolidino)methyl, or (N-

thiomorpholino)methyl." Accordingly, relative to claim 4, the Examiner is identifying the R_1 group of the Freskos compound to be what claim 4 says is:

R_1 is

. . .

d) $-(CH_2)_h-C_{3-8}$ cycloalkyl,

e) $-(CH_2)_h$-aryl,

f) $-(CH_2)_h$-het,

wherein, for the claimed compound to be of the Freskos type, "h" must equal 0. Only when "h" = 0 is the R_1 substituent of claim 4 a 5- or 6-membered cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical **bonded directly to the depicted SO_2 –group** as the Freskos reference requires.

The R_2 group of the Freskos compound is said at page 8 to be "hydridro, C_1-C_4 hydrocarbyl, hydroxyl- C_1-C_4 hydrocarbyl, C_1-C_4 hydrocarbyloxy, halo- C_1-C_4 hydrocarbyl, C_1-C_4 hydrocarbyloxymethyl, aminomethyl, (N-C_1-C_3 hydrocarbyl) aminomethyl, (N, N-di-C_1-C_3 hydrocarbyl) aminomethyl, (N-morpholino)methyl, (N-pyrrolidino)methyl, or (N-thiomorpholino)methyl group."

The R_2 group of current claim 4 is,

R_2 is

d) $-(CH_2)_h-C_{3-8}$ cycloalkyl,

e) $-(CH_2)_h-C_{3-8}$ cycloalkenyl,

f) $-(CH_2)_h$-aryl,

g) $-(CH_2)_h$-het,

h) $-(CH_2)_h$-Q.

Since "h" = 0 the R_2 group of claim 4 reduces to

d) -C_{3-8} cycloalkyl,

e) - C_{3-8} cycloalkenyl,

f) -aryl,

g) -het,

h) -Q.

Hence, in current claim 4, its R_2 group is not and cannot be any of the groups which Freskos names as its R_2 groups, namely, "**hydridro**, **C_1-C_4 hydrocarbyl**, hydroxyl- **C_1-C_4 hydrocarbyl**, **C_1-C_4 hydrocarbyloxy**, halo- **C_1-C_4 hydrocarbyl**, C_1-C_4 hydrocarbyloxy**methyl**, amino**methyl**, (N-C_1-C_3 hydrocarbyl) amino**methyl**, (N, N-di-C_1-C_3 hydrocarbyl) amino**methyl**, (N-morpholino)**methyl**, (N-pyrrolidino)**methyl**, or (N-thiomorpholino)**methyl** group." Nor is there any suggestion in Freskos that would motivate one of ordinary skill in the art to replace a Freskos R_2 group with a C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, aryl, het, or Q group as current claim 4 requires when "h" = 0.

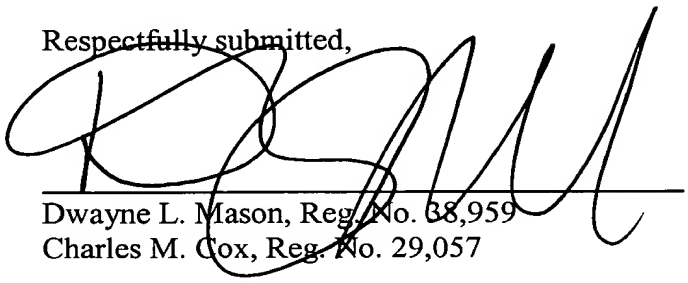
Claim 33 restricts the R_2 group to the groups (d) – (h), wherein "h" equals to a value of 1 or greater. As before noted, when "h" equals to a value of 1 or greater, then one does not have a compound of Freskos et al. (WO 98/39326) which requires a substituent that contains a 5- or 6-membered cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical **bonded directly to the depicted SO_2 –group.**

The scheme 1, page 95 "deprotection" product of the Freskos et al. reference does not apply to the genus of compounds to which claims 35-36 are limited. The "deprotection" product of the Freskos et al. reference requires a hydroxyl group at the "Y" position whereas claim 35 requires a fluoro group and claim 36 requires a NR_9R_{10} group at this "Y" position.

CONCLUSION

The Applicants respectfully submit that this application is now in condition for allowance, in view of the above remarks. Early notification to that effect is earnestly solicited.

Respectfully submitted,



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